

Focus on chlamydia

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The focus on chlamydia in this issue of *STI* is timely. A debate on the second day of the 17th International Society for STD Research and 10th International Union against STI meeting in Seattle on 30 July will address the topic "Epidemiology of chlamydial infection: are we losing ground?" The first "special issue" about sexually transmitted *Chlamydia trachomatis* in this journal, then called the *British Journal of Venereal Diseases*, was published in December 1972 when seven articles examined diagnostic and clinical aspects of a new sexually transmitted infection.¹ Chlamydia is now the most commonly reported of all infections in countries like the USA and Sweden. The papers collected here address new aspects of *C. trachomatis* but also articulate the growing uncertainties about our efforts to control this pathogen.

Screening asymptomatic individuals seems to many people to be the obvious solution to prevent the transmission and adverse consequences of chlamydia,² including preterm delivery and premature rupture of membranes in pregnant women. (see p 314)³ It is also a very expensive solution. (see p 267)⁴ The economic modelling and evaluation study by Adams *et al* shows that it is going to be difficult for the opportunistic strategy being implemented by the National Chlamydia Screening Programme in England to be cost effective. Proactive screening, using population registers to identify and invite people to be screened regularly, is usually assumed to be more expensive to run than opportunistic screening. Robinson *et al*⁵ estimated the health service and patient costs of a postal chlamydia screening approach in England. (see p 276) The cost per invitation was actually similar to that of an organised opportunistic screening programme.⁶

We are learning the hard way that delivering chlamydia screening effectively and efficiently is easier than it sounds.⁷ If we cannot screen a sufficiently high proportion of the target population sufficiently regularly, then chlamydia transmission will not be interrupted and complications will not be prevented.

Repeated infection with chlamydia is increasingly being recognised as a problem in both women and men who have been screened once.^{8,9} (see p 292 and p 304) In a prospective study of women screened in pilot studies for the National Chlamydia Screening Programme in England, LaMontagne *et al* showed that nearly 30% had a repeat infection, mostly within 9 months of the initial diagnosis. Repeat infections were associated with either having a new partner or not having all previous partners treated.⁸ The systematic review of studies in men by Fung *et al* also found untreated partners to be strongly associated with re-infection.⁹ Taken together, these studies suggest that partner notification alone does not reach enough of the sex partners of either women or men to control the spread of infection; in addition, screening interventions need to include men, people who have had a chlamydia infection should be retested, and regular testing is required to detect newly acquired infections. Fung *et al* also make an important methodological point. Prospective studies with active follow-up and high participation rates will give the least biased estimates of the repeat infection rate. Retrospective studies based on records of people returning for treatment services overestimate repeat infection rates because they include symptomatic people who are more likely to be infected, and exclude from the denominator all the people who remained uninfected and the asymptotically infected.

Regular screening should reduce the rate of reinfection. Cook *et al* report a trial that we believe to be the first randomised evaluation of the effects of multiple rounds of screening.¹⁰ (see p 286) They compared two approaches to proactive screening among young women at high risk of chlamydia in the USA: an invitation to attend a clinic or home testing kits delivered at 6 month intervals to the participant's home. Women who received home testing kits were more likely to be tested (1.94 tests per year) than those invited to the clinic (1.41 tests per year). A useful comparison of screening uptake would be with current practice, in which women are screened opportunistically in

clinic settings but do not receive invitations to be rescreened. The challenges now are to see whether increased testing rates result in lower rates of pelvic inflammatory disease and chlamydia prevalence, and whether an intervention like this is feasible on a population level in the USA.

Nucleic acid amplification tests that can be used on non-invasively collected specimens made studies such as those by Cook *et al* and Robinson *et al* possible. These tests, together with recommendations for testing asymptomatic individuals, have had a major impact on rates of diagnostic testing, case-finding, screening and detection in industrialised countries. Hughes *et al* document a striking increase in the rates of chlamydia testing in primary care in the UK from 1998 to 2004, partly due to the new diagnostics, which is not captured by the existing routine surveillance system. (see p 310)¹¹ They also show that few men are currently being tested in primary care. Since the National Chlamydia Screening Programme in England includes sexually active men under the age of 25 years, more opportunities for reaching men are needed. Sripada *et al* offered chlamydia testing to asymptomatic men attending family planning, fracture and fertility clinics in Scotland. (see p 282)¹² In this research study the offer of a chlamydia screening test was well received. In the settings with the highest acceptance rates (fracture and fertility clinics), however, positivity rates were very low. In family planning clinics, where the men were younger, only 55% accepted the offer of a test, but 15% were infected. This might therefore be a promising setting in which to offer screening to men, but the proportion of men eligible for screening who use family planning clinics is likely to be very low. Since general practice remains the single healthcare setting attended by most young men, perhaps more effort should be put into getting young men screened there.¹³

The appearance in Sweden of a new variant of *C. trachomatis* also relates to the advent of nucleic acid amplification tests. (see p 253)¹⁴ The mutant strain escapes detection by two of the most widely used tests. One of the take home lessons from this outbreak is that accurate and timely chlamydia surveillance systems are extremely valuable. The new variant could have gone undetected for much longer if a sudden reversal in a 10 year upward trend in chlamydia rates had not sparked an investigation.¹⁵ This could not be attributed to any improvement in chlamydia control measures so the microbiologists investigated the diagnostic tests. As part of the investigation of this outbreak,

studies among people infected with the new chlamydia variant could contribute enormously to our understanding of the sexual networks through which chlamydia spreads, similar to the insights from empirical studies of outbreaks of penicillinase-producing *Neisseria gonorrhoeae*.¹⁶ We hope that this opportunity will not be missed.

Another challenging variant of chlamydia is described in a paper from the UK. (see p 339)¹⁷ Researchers evaluating a rapid test for chlamydia noticed discrepant results: a sample testing negative on two commercial tests was, in fact, a rare pathogenic plasmid-free chlamydia variant that was resistant to azithromycin. Both reports of variants are timely reminders of the need for vigilance in surveillance and in clinical work, being open to the possibility of missed diagnoses.

Intriguingly, the new Swedish chlamydia variant has not yet spread widely. Maybe it is a matter of time. This contrasts somewhat with the outbreaks of lymphogranuloma venereum (LGV, L2 serovar) in men who have sex with men that were first noticed in the Netherlands but spread to several European countries and North America. Jebbari *et al* provide an update on LGV in the UK, showing that although the outbreak peaked in 2005, the infection is now endemic among men who have sex with men. (see p 324)¹⁸ Proctitis continues to be the most common presentation of LGV in the UK and other European countries, but other syndromes may occur as shown in a case report from France which describes an atypical presentation with "bubonulcus". (see p 337)¹⁹ Investigation of LGV outbreaks has been hampered by diagnostic limitations. In some areas there is limited capacity for diagnosing rectal chlamydia, partly because none of the commercial nucleic acid amplification tests are licensed for use with rectal specimens, but Alexander *et al* show that positive rectal chlamydia tests sent to a reference laboratory were mostly confirmed. (see p 327)²⁰ Van der Snoek *et al* explore the possible contribution of

serological testing to early LGV diagnosis. (see p 330)²¹

Thirty-five years ago this journal was alerting clinicians to the role of chlamydia in different clinical syndromes. Today the pathogenic role of *Mycoplasma genitalium* is being investigated, but is not so clear cut. Jurstrand *et al* did not find any association with pelvic inflammatory disease or ectopic pregnancy. (see p 319)²² They did, however, replicate the known strong associations with *C trachomatis*. We hope that the articles in this issue alert readers to the continued challenges of diagnosis and control, and to the emergence and re-emergence of different variants of chlamydia.

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